



## Images in Sleep Medicine

# RLS with PLMS in a child with hemolytic anemia caused by pyruvate kinase deficiency

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## 1. Introduction to the case

Pyruvate kinase deficiency (PKD) is the most common glycolytic defect causing congenital hemolytic anemia [1]. This rare disease, caused by mutations in the PKLR gene may be misdiagnosed in mild cases [2,3].

An eight-year-old girl previously diagnosed with PKD (genetically confirmed at the age of seven years, after suffering from anemia, jaundice and hemolytic crises since the neonatal period), and attention deficit hyperactivity disorder (ADHD), was referred to our Sleep Unit, complaining of excessive daytime sleepiness, snoring and restless sleep. She complained about unpleasant sensations in legs during rest and restlessness at night, fulfilling criteria for restless legs syndrome (RLS).

Neurological and general examination were normal. Anthropometric measurements: weight 30.6 Kg, height 130 cm, and body mass

index (BMI) 18 kg/m<sup>2</sup>. Her Pediatric Daytime Sleepiness Scale score was 22. Neuropsychological assessment showed an impairment in executive functions, and sustained attention difficulties with hyperactivity.

Laboratory results were as follows: hemoglobin 10.9 g/dl (11.5–15.5), reticulocytes 12% (0.5–1.5), ferritin 236 µg/L (12–200), transferrin 182 mg/dl (200–360), transferrin saturation index 39% (15–45%), and soluble transferrin receptor (STR) 20 mg/L (1.90–4.40). Furthermore, her vitamin B12 measured 323 µg/L (200–980); folate 11.7 µg/L (2.5–15) and bilirubin 3.2 mg/dl (0.1–1.1). In addition, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT) and C-reactive protein (CRP) levels were normal.

Abdominal ultrasound, and 1.5 T brain magnetic resonance imaging (MRI [Ethical Committee approval and written informed consents provided]) were normal, ruling out the presence of hemosiderosis.

Psychiatric treatment consists of sustained release methylphenidate 37 mg/d. One year later, RLS (due to an intermittent course) and ADHD symptoms had improved, leading to a better performance at school.

## 2. Image analysis

Polysomnography (PSG, Fig. 1) showed a disrupted and fragmented sleep with prolonged sleep latency (56 min), reduction of rapid eye movements (REM, 9.6%), elevated wake after sleep onset (WASO, 51 min), and reduced sleep efficiency (88%); periodic leg movements during sleep (PLMs) index was 33.4/h. Respiratory sleep disorders were ruled out.

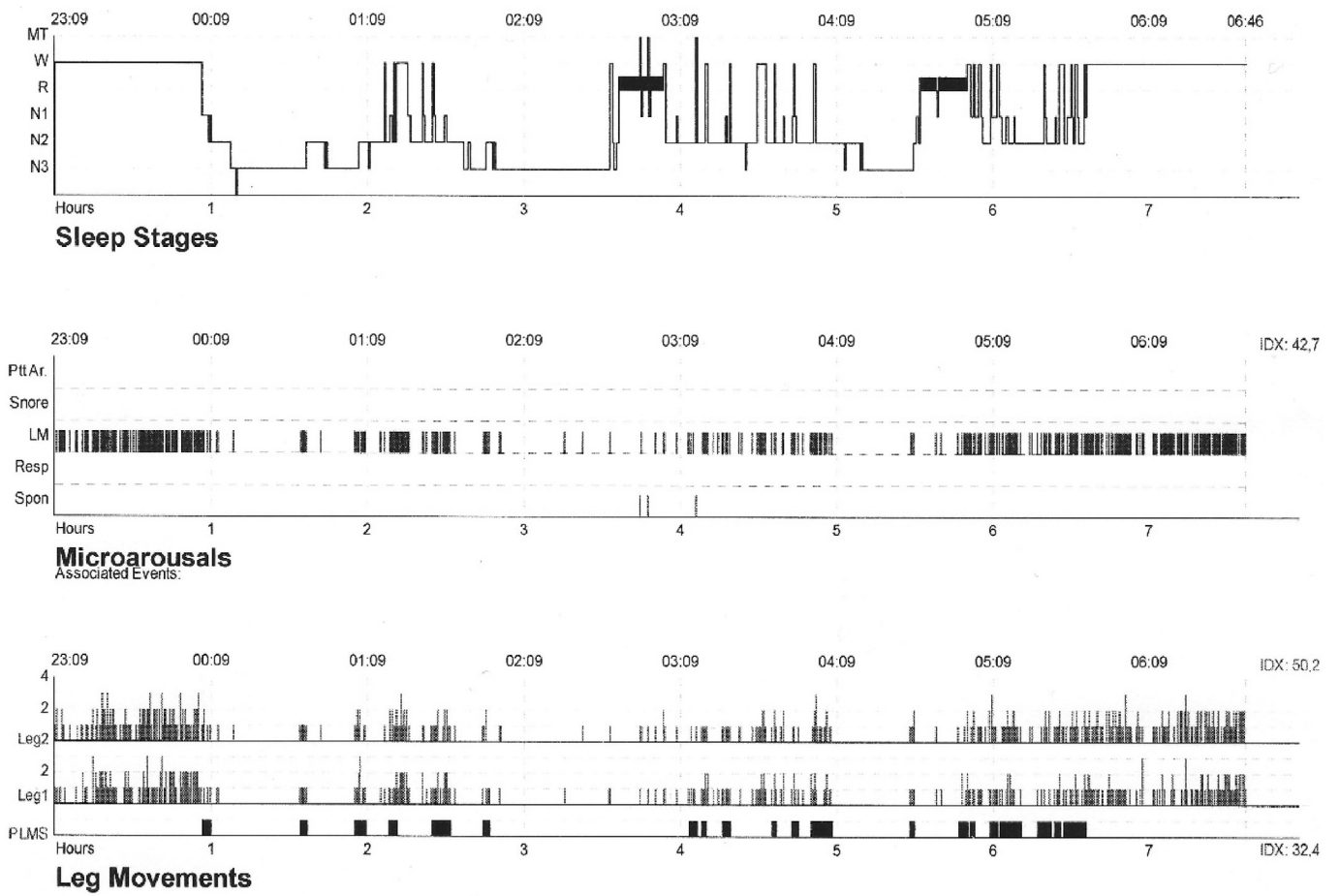
One year later, a new PSG (Fig. 2) showed an improvement in sleep efficiency (96%), sleep latency (35 min), PLMs index (11.6/h) and WASO (13 min).

## 3. Discussion

Sleep deprivation secondary to RLS can exacerbate anemia symptoms, as fatigue, and those of ADHD. We emphasized the importance of screening for the presence of RLS in children

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**Fig. 1.** First PSG showed a disrupted and fragmented sleep, with a long sleep latency, reduced sleep efficiency, and a high rate of PLM index.

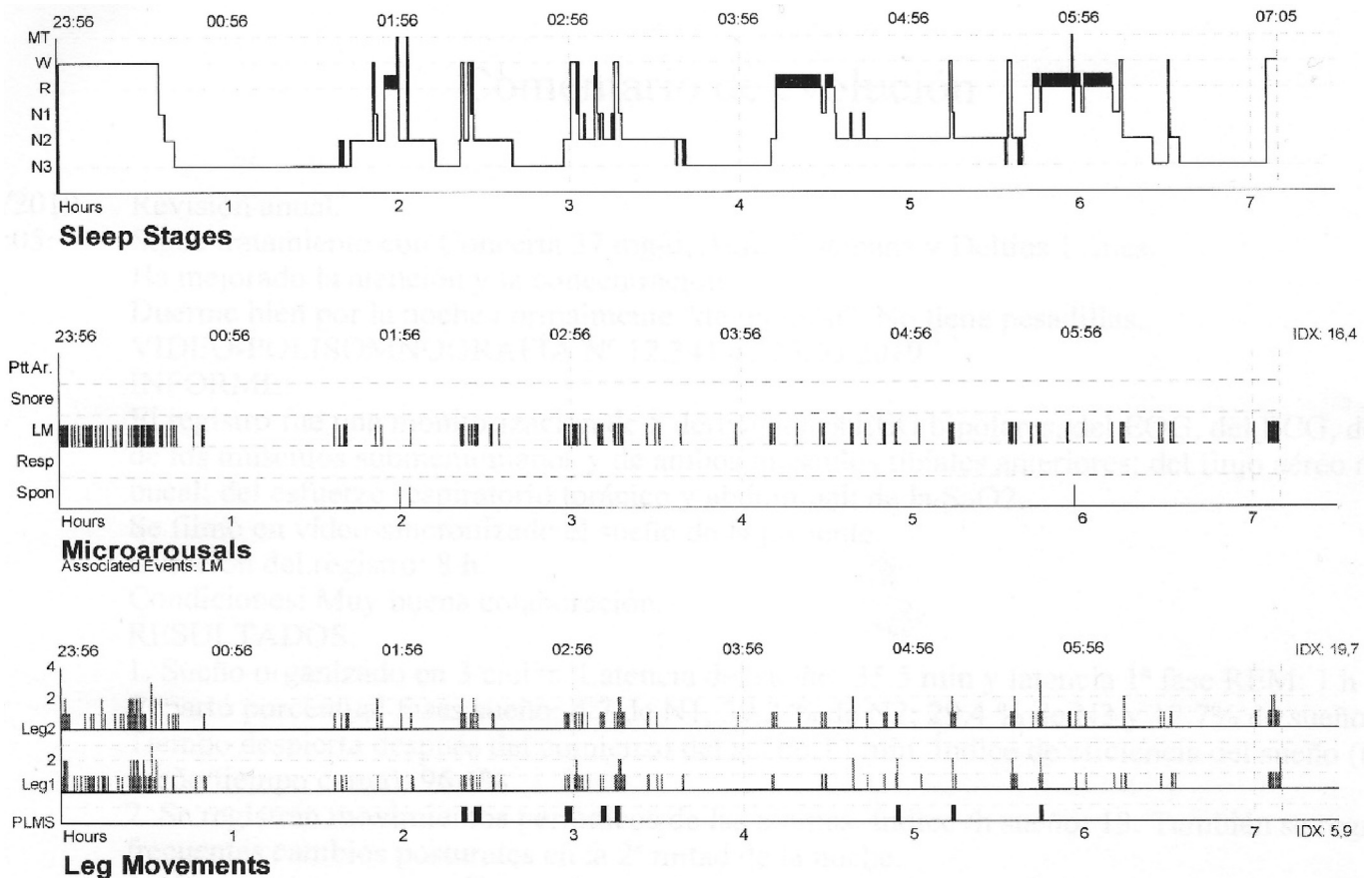


Fig. 2. One year later PSG parameters have improved, showing a shorter sleep latency, reduced WASO and lower PLM index.

with anemia, even in those with hyperferritinemia, as in this case.

The risk of ADHD in RLS patients is well known and RLS with PLMs is one of the phenotypes of ADHD in childhood. A disorder of iron metabolism probably underlies both diseases. Iron deficiency anemia in childhood has been linked to PLMs [4] and to ADHD [5].

The hemolytic and regenerative processes underlying RLS and ADHD in the patient were associated with anemia, hyperferritinemia, and high STR. When abnormal red cell travel through the splenic capillaries are damaged and are partially cleared by the spleen and liver. Iron cannot be removed and is accumulated in the liver and an elevated ferritin levels appeared. Iron treatment is contraindicated, because it would rise the risk of hemosiderosis.

MRI and other brain iron measures have limited sensitivity because of the lack of information about iron central nervous system status in childhood anemias. A 3 T MRI, not available in our center, would allow quantifying the brain iron content in several structures. Further studies are warranted to quantify brain iron concentration in children with hemolytic anemia and RLS.

#### Conflict of interest

Nothing to disclose.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: <https://doi.org/10.1016/j.sleep.2020.01.013>.

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